

WHAT IS CLAIMED IS:

1. A method for determining whether a first protein interacts with a second protein within a living cell, the method comprising:

a) providing the first protein complexed to a donor luciferase and the second protein complexed to an acceptor fluorophore within the cell;

b) placing the complexed first protein and the complexed second protein in proximity to each other within the cell; and

c) detecting any fluorescence from the acceptor fluorophore;

where the donor luciferase is capable of luminescence resonance energy transfer to the acceptor fluorophore when the first protein is in proximity to the second protein; and

where fluorescence of the acceptor fluorophore resulting from luminescence resonance energy transfer from the donor luciferase indicates that the first protein has interacted with the second protein.

2. The method of claim 1, where providing the first protein complexed to a donor luciferase and the second protein complexed to an acceptor fluorophore comprises genetically engineering DNA and transferring the genetically engineered DNA to the living cell causing the cell to produce the first protein complexed to a donor luciferase and the second protein complexed to an acceptor fluorophore.

3. The method of claim 1, where the cell provided with the first protein complexed to a donor luciferase is a mammalian cell.

4. The method of claim 1, where the cell provided with the second protein complexed to a acceptor fluorophore is a mammalian cell.

5. The method of claim 1, where the donor luciferase provided is *Renilla* luciferase.

6. The method of claim 1, where the acceptor fluorophore provided is a green fluorescent protein.

7. The method of claim 1, where the acceptor fluorophore provided is an *Aequorea* green fluorescent protein.

8. The method of claim 1, where detecting any fluorescence from the donor luciferase is performed using spectrofluorometry.

9. A method for determining whether a first molecule interacts with a second molecule within a living cell, the method comprising:

a) providing the first molecule complexed to a donor luciferase and the second molecule complexed to an acceptor fluorophore within the cell;

b) placing the complexed first molecule and the complexed second molecule in proximity to each other within the cell; and

5 c) detecting any fluorescence from the acceptor fluorophore;

where the donor luciferase is capable of luminescence resonance energy transfer to the acceptor fluorophore when the first molecule is in proximity to the second molecule; and

where fluorescence of the acceptor fluorophore resulting from luminescence resonance energy transfer from the donor luciferase indicates that the first molecule has interacted with
10 the second molecule.

10. The method of claim 9, where the first molecule is a first protein and where the second molecule is a second protein; and

where providing the first protein complexed to a donor luciferase and the second protein complexed to an acceptor fluorophore comprises genetically engineering DNA and
15 transferring the genetically engineered DNA to the living cell causing the cell to produce the first protein complexed to a donor luciferase and the second protein complexed to an acceptor fluorophore.

11. The method of claim 10, where the cell provided with the first protein complexed to a donor luciferase is a mammalian cell.

20 12. The method of claim 10, where the cell provided with the second protein complexed to a acceptor fluorophore is a mammalian cell.

13. The method of claim 9, where the donor luciferase provided is *Renilla* luciferase.

14. The method of claim 9, where the acceptor fluorophore provided is a green fluorescent protein.

25 15. The method of claim 9, where the acceptor fluorophore provided is a *Aequorea* green fluorescent protein.

16. The method of claim 9, where detecting any fluorescence from the donor luciferase is performed using spectrofluorometry.

17. A method for determining whether a first protein interacts with a second protein,
30 the method comprising:

a) providing the first protein complexed to a donor luciferase and the second protein

complexed to an acceptor fluorophore;

b) placing the complexed first protein and the complexed second protein in proximity to each other; and

c) detecting any fluorescence from the acceptor fluorophore;

5 where the donor luciferase is capable of luminescence resonance energy transfer to the acceptor fluorophore when the first protein is in proximity to the second protein; and

where fluorescence of the acceptor fluorophore resulting from luminescence resonance energy transfer from the donor luciferase indicates that the first protein has interacted with the second protein.

10 18. The method of claim 17, where providing the first protein complexed to a donor luciferase and the second protein complexed to an acceptor fluorophore comprises genetically engineering DNA and transferring the genetically engineered DNA to a living cell causing the cell to produce the first protein complexed to a donor luciferase and the second protein complexed to an acceptor fluorophore.

15 19. The method of claim 18, where the cell provided with the first protein complexed to a donor luciferase is a mammalian cell.

20. The method of claim 18, where the cell provided with the second protein complexed to a acceptor fluorophore is a mammalian cell.

20 21. The method of claim 17, where the donor luciferase provided is *Renilla* luciferase.

22. The method of claim 17, where the acceptor fluorophore provided is a green fluorescent protein.

23. The method of claim 17, where the acceptor fluorophore provided is an *Aequorea* green fluorescent protein.

25 24. The method of claim 17, where detecting any fluorescence from the donor luciferase is performed using spectrofluorometry.

25. A method for determining whether a first molecule interacts with a second molecule, the method comprising:

30 a) providing the first molecule complexed to a donor luciferase and the second molecule complexed to an acceptor fluorophore;

b) placing the complexed first molecule and the complexed second molecule in

proximity to each other; and

c) detecting any fluorescence from the acceptor fluorophore;

where the donor luciferase is capable of luminescence resonance energy transfer to the acceptor fluorophore when the first molecule is in proximity to the second molecule; and

5 where fluorescence of the acceptor fluorophore resulting from luminescence resonance energy transfer from the donor luciferase indicates that the first molecule has interacted with the second molecule.

26. The method of claim 25, where the first molecule is a first protein and where the second molecule is a second protein; and

10 where providing the first protein complexed to a donor luciferase and the second protein complexed to an acceptor fluorophore comprises genetically engineering DNA and transferring the genetically engineered DNA to a living cell causing the cell to produce the first protein complexed to a donor luciferase and the second protein complexed to an acceptor fluorophore.

15 27. The method of claim 26, where the cell provided with the first protein complexed to a donor luciferase is a mammalian cell.

28. The method of claim 26, where the cell provided with the second protein complexed to a acceptor fluorophore is a mammalian cell.

20 29. The method of claim 25, where the donor luciferase provided is *Renilla* luciferase.

30. The method of claim 25, where the acceptor fluorophore provided is a green fluorescent protein.

31. The method of claim 25, where the acceptor fluorophore provided is a *Aequorea* green fluorescent protein.

25 32. The method of claim 25, where detecting any fluorescence from the donor luciferase is performed using spectrofluorometry.